

### REMARKS

Applicants respectfully requests entry of the amendments and remarks submitted herein. Claims 21, 30-32, 42 and 45 are amended, claims 1-20 and 44 are canceled, and claims 46-71 are added. Therefore, claims 21-43 and 45-71 are currently pending. Applicants submit that the amendments to the claims and the new claims do not introduce new matter.

#### I. The Obviousness-type Double Patenting Rejection

The Examiner rejected claims 21-25, 27-30 and 45 under the judicially created doctrine of obviousness-type double patenting over claims 1 and 189 of co-pending U.S. Application Serial No. 09/154,830 (the '830 application).

A petition decision mailed on November 16, 2005 in the '830 application states that the '830 Application was revived solely for purposes of continuity, but once continuity was established, the '830 Application was again abandoned in favor of continuing U.S. Application Ser. No. 10/937,746, filed September 9, 2004. As the '830 application is abandoned, Applicants request that this rejection be withdrawn.

#### II. The 35 U.S.C. § 112, Second Paragraph Rejections

The Examiner rejected claims 21-38, 42-43 and 45 under 35 U.S.C. § 112, second paragraph, alleging that those claims are indefinite for failing to particularly point out and distinctly claim the subject matter that the application regards as the invention. As these rejections may be maintained with respect to the pending claims, they are respectfully traversed.

(1) The Examiner alleges that the term "substantially" in claims 21, 32 and 45 is relative, and that the recitation of this term renders the claim indefinite. Applicants respectfully disagree. However, as amended, claims 21, 32 and 45 do not recite the term "substantially". New claims 46 and 71 recite the phrase "substantially undegraded RNA". At page 12, lines 7-15 of the specification, Applicants define the phrase "substantially undegraded RNA". Thus, Applicants respectfully submit that the phrase "substantially undegraded RNA", in view of the specification, is definite.

(2) The Examiner alleges that the term "preferentially" in claims 21 and 45 renders those claims indefinite. Applicants respectfully disagree. In claims 21 and 45, the term "preferentially" is used to indicate that nucleic acids preferentially bind to the solid support and

that RNA is preferentially eluted from the solid support. As is described in the specification, *e.g.*, at page 8, lines 6-9, nucleic acids released following lysis preferentially bind to a solid support of choice over other contaminants such as proteins and phospholipids. Further, as described at page 17, lines 6-8, RNA bound to the solid support is preferentially eluted using an RNA elution solution while leaving the contaminating DNA bound to the solid support. In other words, RNA is more selectively bound to the support in comparison with proteins and phospholipids and more selectively eluted therefrom in comparison with DNA. Thus, Applicants respectfully submit that the term "preferentially", in view of the specification, is definite.

(3) The Examiner alleges that the limitation in claim 31 of "the strong chaotropic substance" of claim 21 does not have adequate antecedent basis. Applicants respectfully disagree. However, to expedite prosecution, claim 31 is amended to remove the phrase "the strong chaotropic substance".

(4) The Examiner alleges that the limitation in claims 42 and 43 of "the RNA binding solution" of claim 21 does not have adequate antecedent basis. Claim 42 is amended to recite that the RNA Lysing Solution of claim 21 comprises a chelating agent. Claim 43 depends from claim 42.

(5) The Examiner alleges that the phrase "such that" in claims 21(c) and 45(a) renders those claim indefinite. Applicants respectfully disagree. However, to expedite prosecution, claims 21 and 45 are amended to remove the phrase "such that".

In view of the above, Applicants request that the rejections under 35 U.S.C. §112, second paragraph, be withdrawn.

### III. Claim Objections

The Examiner objected to claims 39-41 as being dependent on non-elected claim 20. Claim 39 is amended to depend from elected claim 21. Claims 40 and 41 depend directly or indirectly from claim 39.

### IV. The 35 U.S.C. § 103(a) Rejection

The Examiner rejected claims 21-38 and 45 under 35 U.S.C. § 103(a), alleging that those claims are unpatentable over Heath (U.S. Patent No. 5,973,137) in combination with Wiggins

(U.S. Patent No. 5,637,687) and Kuroita *et al.* (U.S. Patent 5,990,302). As this rejection may be maintained with respect to the pending claims, it is respectfully traversed.

Independent claim 21 recites a method for purifying RNA from biological material comprising RNA, comprising the steps of: (a) mixing said biological material with an RNA Lysing Solution buffered at a pH of greater than about 7, said RNA Lysing Solution comprising an amphiphillic reagent, and an RNA complexing salt, wherein said RNA Lysing Solution is free of a strong chaotropic substance; (b) lysing said biological material with said RNA Lysing Solution to form a lysate comprising nucleic acids comprising RNA and non-nucleic acid biological matter; (c) contacting said lysate to an immobilized non-silica solid support, wherein said nucleic acids comprising RNA in said lysate preferentially bind to said solid support; (d) washing said solid support with an RNA wash solution to remove non-nucleic acid biological matter; and (e) preferentially eluting the bound RNA from said solid support with an RNA elution solution to obtain the RNA. Claims 22-38 depend directly or indirectly from claim 21.

Independent claim 45 recites a method for purifying RNA from biological material, comprising the steps of: (a) contacting a biological material containing RNA with a solid support pre-treated with an RNA Lysing Solution buffered at a pH of greater than about 7, wherein the RNA Lysing Solution is bound to the solid support, said RNA Lysing Solution comprising an amphiphillic reagent and an RNA-complexing salt, wherein said RNA Lysing Solution is free of a strong chaotropic substance; (b) contacting said biological material to said solid support in order to release nucleic acids comprising RNA and non-nucleic acid biological matter causing nucleic acids comprising RNA to preferentially bind to said solid support; (c) washing said solid support with an RNA wash solution to remove biological materials other than bound nucleic acids comprising RNA; and (d) preferentially eluting the bound RNA from said solid support with an RNA elution solution to obtain the RNA.

A rejection of obviousness under 35 U.S.C. § 103 requires that the Examiner establish a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, the Examiner has the burden to establish three basic elements. First, the Examiner must establish that there is some suggestion or motivation, either in the cited documents themselves or in the knowledge generally available to an art worker, to modify the documents or to combine document teachings so as to arrive at the claimed invention. Second, the Examiner must establish that there is a reasonable expectation of success. Finally, the Examiner must establish that the prior art

documents teach or suggests all the claim limitations. M.P.E.P. § 2143. Applicants respectfully submit that the Examiner has not demonstrated that the claims are *prima facie* obvious in view of the cited documents because the Examiner has not demonstrated that there is some suggestion or motivation to modify the documents or to combine document teachings so as to arrive at the claimed invention.

The primary document Heath relates to an RNA isolation process that utilizes low pH reagents. (*see, e.g.*, the Title and the Abstract) For example, Heath relates to the use of a “cell lysis reagent” at a pH of less than about 6, preferably less than about 5, and more preferably less than about 4. (*see* column 3, lines 49-59 and claims 1 and 12) Heath also states that a “cell suspension reagent” can be combined with a biological sample to form a cell suspension that keeps the cells intact while their cell walls are digested by a lytic enzyme that digests  $\beta$ -1,3-glucose polymers. (*see* column 8, lines 28-60) The process of Heath may also include the use of a “protein-DNA precipitation reagent” and centrifugation to separate the RNA from the DNA and proteins. (*see* column 3, lines 60-65 and column 10, lines 52-58)

The secondary document Wiggins relates to methods and compositions for isolating nucleic acids that involve the use of combinations of chaotropic agents. (*see, e.g.*, the Abstract; column 6, lines 46-56; and column 6, line 63 through column 7, line 7). For isolating RNA, Wiggins teaches that the most preferred composition for isolating RNA uses three chaotropic agents. (column 7, lines 11-14) Wiggins teaches that for isolating RNA, the pH of the solution is acidic, preferably from about 4 to 6, more preferably 5. (*see* column 9, lines 44-47)

The secondary document Kuroita *et al.* relates to methods and reagents for isolating RNA using an acidic solution and chaotropic agents. (*see, e.g.*, the Abstract; column 2, lines 45-50; and column 3, lines 51-54) Kuroita *et al.* states that the solution has a pH of not more than 6.0, and that an acetate buffer or citrate buffer having a pH of 3-4 is most preferably used. (column 4, line 65 through column 5, line 8)

Applicants respectfully submit that the Examiner has not demonstrated that the claims are *prima facie* obvious in view of the cited documents because the Examiner has not demonstrated that there is some suggestion or motivation to modify the documents or to combine document teachings so as to arrive at the claimed invention. Further, even if for the sake of argument the documents contain the claim limitations, Applicants respectfully submit that the Examiner has improperly used hindsight to combine the teachings to arrive at the claimed invention.

The primary document Heath relates to the use of a "cell lysis reagent" at a pH of less than about 6, preferably less than about 5, and more preferably less than about 4. In contrast, the present claims recite that RNA lysing solution is buffered at a pH of greater than about 7. Even if, for the sake of argument, Heath states that others may have used lysing reagents having a pH of more than 7, Applicants respectfully submit that Heath teaches the art worker to use a lysing solution having a pH of less than about 6 and does not teach or suggest that a pH of greater than 7 should be used in their methods or compositions. Further, the Examiner states that Heath does not obtain the RNA from the solution using a solid support.

Wiggins relates to methods and compositions for isolating nucleic acids that involve the use of combinations of chaotropic agents. In contrast, the claims of the present invention recite that the RNA Lysing Solution is free of a strong chaotropic substance. Thus, Applicants respectfully submit that Wiggins teaches away from excluding chaotropic agents from the lysing solution. Further, Wiggins teaches that for isolating RNA, the pH of the solution is acidic, preferably from about 4 to 6, more preferably 5, thereby teaching away from the use of an RNA lysing solution buffered at a pH of greater than about 7, as is presently claimed.

Similarly to Wiggins, Kuroita *et al.* relates to methods and reagents for isolating RNA using an acidic solution and chaotropic agents. Kuroita *et al.* states that the solution has a pH of not more than 6.0, and that an acetate buffer or citrate buffer having a pH of 3-4 is most preferably used. Applicants submit that Kuroita *et al.* also teaches away from excluding chaotropic agents from the lysing solution and the use of an RNA lysing solution buffered at a pH of greater than about 7.

Thus, Applicants respectfully submit that the combination of Heath, Wiggins, Kuroita *et al.* teaches away from the presently-claiming invention, *e.g.*, by instructing the art worker to use acidic lysing solutions that contain chaotropic agents. Accordingly, Applicants respectfully request withdraw of this rejection of the claims under 35 U.S.C. § 103.

Applicant : Ellen M. Heath et al.  
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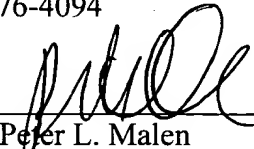
Attorney's Docket No.: 17094.002US1

### CONCLUSION

The Examiner is invited to contact Applicants' Representative at the below-listed telephone number if there are any questions regarding this Response or if prosecution of this application may be assisted thereby. If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 50-3503. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extension fees to Deposit Account 50-3503.

Respectfully submitted,  
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